

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 22 JUL 2005

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Applicant's or agent's file reference 22307 WO-BUR		<b>FOR FURTHER ACTION</b>		See Form PCT/IPEA/416
International application No. PCT/EP2004/013627		International filing date (day/month/year) 01.12.2004	Priority date (day/month/year) 02.12.2003	
International Patent Classification (IPC) or national classification and IPC C12Q1/68, C07H21/00				
Applicant ROCHE DIAGNOSTICS GMBH et al.				
<p>1. This report is the International preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (Indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  17.03.2005		Date of completion of this report  21.07.2005		
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer  Bardili, W  Telephone No. +49 89 2399-2132		



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/013627

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1-33 as originally filed

**Claims, Numbers**

1-14 as originally filed

**Drawings, Sheets**

1/4-4/4 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/013627

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-14
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-14
Industrial applicability (IA)	Yes: Claims	1-14
	No: Claims	

**2. Citations and explanations (Rule 70.7):**

**see separate sheet**

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

DE-A-100 50 942 discloses a method to detect methylation of cytosine in DNA samples wherein the cytosine bases of the DNA are deaminated and converted to uracil bases. The deamination is effected by sodium sulfite or hydrogen sulfite treatment of the DNA and subsequent alkaline hydrolysis of the intermediate sulfite cytosine adducts (see example 1). Novelty of the claimed method to convert cytosine bases to uracil bases in a nucleic acid is recognised in view of the fact that guanidinium hydrogen sulfite is used in the deamination of cytosine.

The applicants submit that "guanidinium hydrogen sulfite can replace the standard deamination reagent showing a somewhat better performance" (page 19 of the description). The table at page 19 of the description, however, shows only that the difference in the mean  $C_T$  values between the prior art and the claimed method is about the same as within each set of experiments 1-5 for each of the individual sulfite reagents (approximately 0.4). Hence, the comparative examples do not indicate a significant improvement over D1. The object of the invention can therefore only be seen in the provision of a further method to deaminate cytosine in DNA. Since the deamination reaction and the intermediates involved were well-known before the filing date of the application it was obvious to a skilled person that the sodium ion of the sulfite reagent was not essential to the reaction and could be replaced with another positive ion, for instance the guanidinium ion. Inventive step therefore cannot be acknowledged.